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Acoustic characterization of antibubbles for quantitative imaging

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Introduction

Traditional ultrasound contrast agents consist of gas microbubbles with a stabilizing shell. Theoretical analysis has shown that adding a sufficiently large liquid core to a gas bubble enhances nonlinear oscillation and, therefore, strongly increases nonlinear behavior [1, 2]. Such bubbles with a liquid core are referred to as **antibubbles**. This work presents a comparison of the **harmonic response of antibubbles** to that of identical bubbles without a liquid core (reference bubbles) and SonoVue (Bracco). The contrast agents were insonified at frequencies of 1 MHz and 2.25 MHz at a range of mechanical indexes (MI) from 0.1 to 0.3. Furthermore, a **dynamic measurement** of indicator dilution curves (IDCs) was conducted with a Vantage system (Verasonics, Inc., Kirkland, WA, USA), evaluating the IDC enhancement.

Methodology

1) Harmonic response

Transmission of 20-cycle pulses, rectangular envelope

Frequency, MHz	Source (diameter, focal distance, central frequency)	Planar piston receiver (diameter, central frequency)
1	V302-SU-F (2.54 cm, 6.35 cm, 1 MHz), Olympus	C304-SU (2.54 cm, 2.25 MHz), Olympus
2.25	V304-SU (2.54 cm, 6.55 cm, 2.25 MHz), Olympus	V307-SU (2.54 cm, 5 MHz), Olympus

Table 1. Characteristics of the sources and receivers utilized for the measurement of the harmonic response

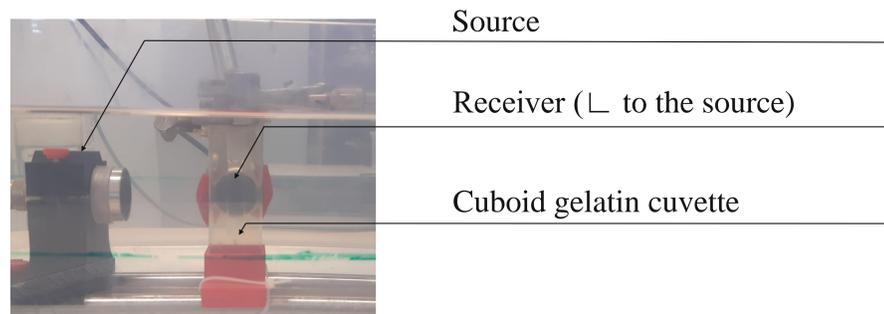


Figure 1. Set up for measurement of the harmonic response

- Reference measurement with 3-4 mL of saline in a gelatin cuboid phantom placed in the focal region of the source
- Contrast agent measurement: Freeze dried material diluted in saline (Baxter B.V. Utrecht, Netherlands) and injected into the cuvette with saline to achieve a concentration of 1 mg/3.5mL.

2) Dynamic measurement

Transmit frequency: 3.5 MHz, contrast mode (pulse inversion+ amplitude modulation)

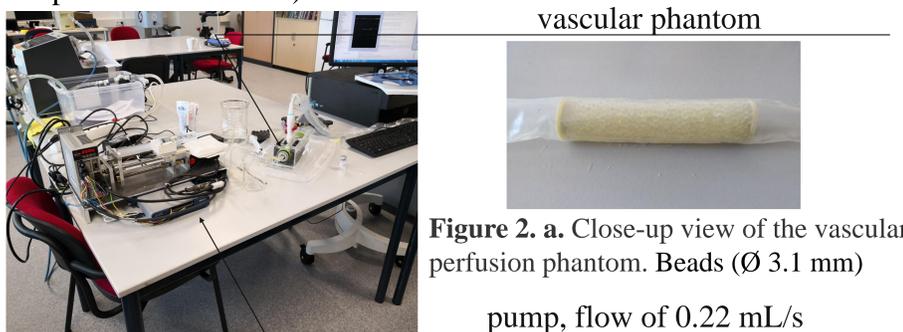


Figure 2. Set up for the dynamic measurement, performed with the Vantage system, probe L11-4

Results

1) Harmonic response

- 1 MHz

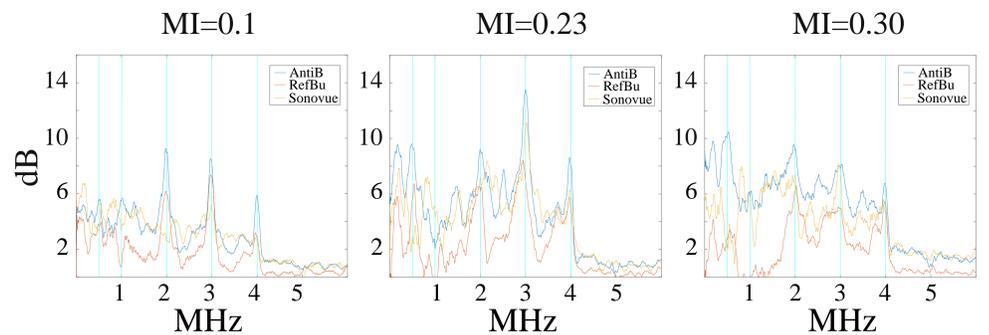


Figure 3. Harmonic response of antibubbles, reference bubbles and SonoVue to insonification with 1 MHz at MIs of 0.1, 0.23 and 0.3 (left to right).

- 2,25 MHz

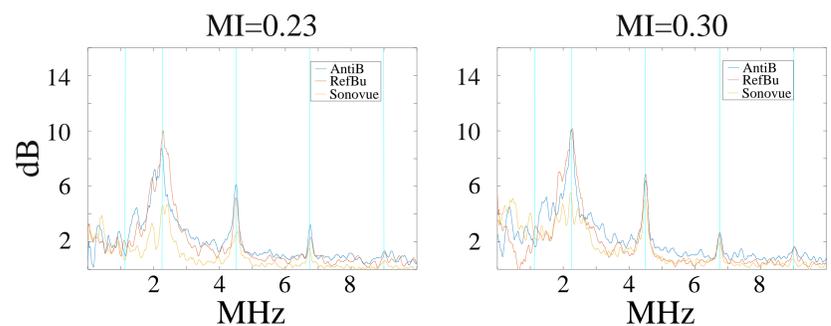


Figure 4. Harmonic response of antibubbles, reference bubbles and SonoVue to insonification with 2,25 MHz at MIs of 0.23 and 0.3 (left to right).

2) Dynamic measurement

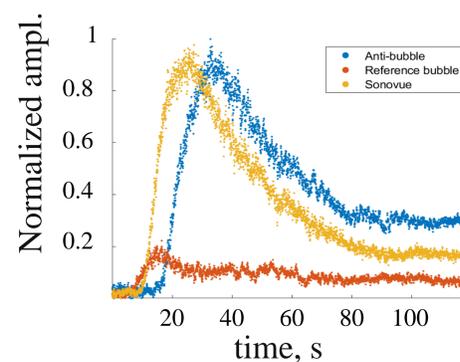


Figure 5. IDCs of antibubbles, reference bubbles and SonoVue.

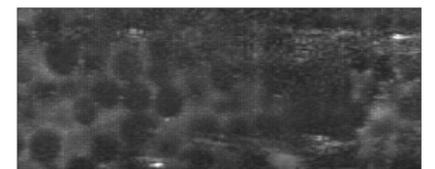


Figure 5. a. Example of a maximum intensity projection image of the vascular phantom (Fig. 2.a.) for SonoVue.

Contrast agent	Enhancement, dB
Antibubbles	89
Refbubbles	66
Sonovue	95

Table 2. Enhancement of IDCs of contrast agents

Conclusion

Antibubbles generate stronger harmonic signal compared to reference bubbles and SonoVue at the frequency of 1 MHz. All studied contrast agents exhibit a comparable response at 2.25 MHz. The dynamic measurement performed at 3.5 MHz showed antibubbles to have a high enhancement, comparable to that of SonoVue. The acquired harmonic responses demonstrate antibubbles' potential for their use as contrast agents in the clinic.

- [1] S. Kotopoulis, K. Johansen, O. H. Gilja, A.T. Poortinga, M. Postema, Acta Physica Polonica A, 127, 99-102.
[2] M. Postema, A. Novell, A.T. Poortinga, A. Bouakaz, Applied Acoustics, 13, 148-150.